

polypeptide comprising the amino acid sequence of SEQ ID NO: 2; or (2) a nucleic acid molecule comprising the coding region of the nucleotide sequence of SEQ ID NO: 1.

#### REMARKS

##### The Amendments

Applicants have cancelled claims 40-41, 53-63 and 71, amended claims 29-32, 35 and 37 and added claims 72-75. Thus, claims 29-35, 37, 48, 64-70 and 72-75 are pending.

Applicants have amended claims 29 and 31 to recite that the nucleic acid molecule is foreign and has a sequence identity of at least 80% to a nucleic acid molecule coding for a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 or to a nucleic acid molecule comprising the coding region of the nucleotide sequence of SEQ ID NO: 1. Support for these amendments may be found throughout the specification. See, e.g., page 8, lines 7-12 and page 10, lines 19-24. Applicants have further amended claims 29 and 31 to improve their form. Applicants have amended claim 30 to correct its dependency in light of the claim amendments and cancellations and have amended claim 32 to delete its recitation of ribozymes. Applicants have amended claim 35 to recite particular harvestable parts of a plant and have amended claim 37 to clarify that the propagation material of a plant comprises a transgenic plant cell. Support for the amendments to claims 35 and 37 is found on page 25, line 24 to page 26, line 5.

Support for added claim 72 is found throughout the specification and in claim 29 as originally filed. Support for added claims 73-74 is found throughout the

specification. See, e.g., originally-filed claim 31 and page 8, lines 7-12. None of the amendments adds new matter. Their entry is requested.

Applicant reserves the right to continue to prosecute and to obtain claims to the cancelled subject matter in other applications claiming priority herefrom.

#### The Election/Restriction

Applicants affirm their election of Group VIII, which was made without traverse in their September 3, 2002 response.

#### The Claim Objections

The Examiner has objected to claims 32 and 59 because the non-elected invention should be deleted from the claims. Applicants traverse.

Applicants have cancelled claim 59, thus obviating this rejection. Applicants will delete the non-elected subject matter in claim 32 upon notice that the claims are otherwise in condition for allowance. Applicants respectfully note that the non-elected invention in claim 32 is drawn to subject matter that should be examined upon allowance of claim 31, which links inventions VIII, XII and XIII. Applicants further note that claims 29-30, 33-34, 48, 64-70 and 72-75 also link inventions VIII, XIII and XIV. Thus, the non-elected invention in claim 32 should also be examined upon allowance of any one of claims 29-31, 33-34, 48, 64-70 or 72-75.

#### The Sequence Listing

Applicants acknowledge that their CRF and paper sequence listing has been entered.

### The Information Disclosure Statement

Applicants acknowledge that an initialed and dated copy of applicants February 8, 2001 Information Disclosure Statement is attached.

### The Double Patenting Rejection

The Examiner has rejected claims 29-35, 37, 48, 53-61, and 64-71 under the judicially created doctrine of obviousness-type double patenting, as allegedly being unpatentable over claims 1-16 of United States Patent No. 6,218,142 (hereafter “the ‘142 patent”). The Examiner states that although the conflicting claims are not identical, they are not patentably distinct from each other because the species claims of the ‘142 patent renders the genus claims of the instant application obvious. Specifically, the Examiner contends that the host cell of the ‘142 patent, which may be a plant cell, makes obvious the transgenic plant cell of claim 29, which has been transformed with SEQ ID NO:1. Applicants traverse in part.

The ‘142 patent issued from United States Application No. 08/811,583 (hereafter “the ‘583 application”), filed March 5, 1997. In a February 25, 1999 restriction requirement in the ‘583 application, the Examiner restricted originally-filed claims 1-12 (designated Group I in that restriction requirement) from originally-filed claims 29-38 (designated Group VIII). Originally-filed claim 11 recited that the host cell may be, *inter alia*, a plant cell comprising a nucleic acid molecule of the invention, while originally-filed claim 29 recited a transgenic plant cell comprising a nucleic acid molecule of the invention. The instant divisional application was filed as a result of the February 25, 1999 restriction

requirement. 35 U.S.C. § 121 prohibits using a patent issuing on an application in which a restriction requirement has been made as a reference in a double patenting rejection. See, e.g., Manual of Patent Examining Procedure (MPEP) 804.01 and the third sentence of 35 U.S.C. § 121. Thus, it is improper to impose a double patenting rejection on the currently-pending claims, all of which are drawn to transgenic plant cells and plants that were encompassed by Group VIII of the February 25, 1999 restriction requirement.

#### The Rejections Under 35 U.S.C. § 101

The Examiner states that claims 35 and 37 are rejected under 35 U.S.C. § 101 as allegedly being directed to non-statutory subject matter. Specifically, the Examiner states that seeds and propagules of transgenic plants have undergone Mendelian segregation and, unless grown under selective conditions, may not have received the transgene. The Examiner contends that this would result in wild-type seed, which is a product of nature.

Applicants have amended claims 35 and 37 to recite that the claimed plant parts comprise the transgenic plant cell, thus obviating the rejection.

#### The Rejections Under 35 U.S.C. § 112, Second Paragraph

The Examiner states that claims 29-35, 37, 48, 53-61, and 71 are rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner's six specific rejections are addressed individually below.

(1) The Examiner states that claims 29(a), 31 and 32 are unduly alternative in reciting “and/or” on one or more occasions. Applicants have amended the claims to remove the “and/or” language, thus obviating the objection.

(2) The Examiner states that claim 29 is confusing in that it recites a “template” serving as a “template.” The Examiner suggests reciting a “first” and “second” template. The Examiner has further stated that “said” lacks antecedent basis. Applicant has amended claim 29 to remove 29(b) and have recast it as added claim 72. Added claim 72 no longer refers to a “template” serving as a “template” and provides antecedent basis for “said.”

(3) The Examiner states that claims 29 and 31 contain parentheticals which are unclear. Applicant traverses. The language of the parentheticals mirrors that of the ‘142 patent, issued from the ‘583 application, which is the parent of the present application, and is clear to one of ordinary skill in the art. Further, changing the wording of the parentheticals would further be confusing in light of the ‘142 patent. Therefore, applicants request that the Examiner withdraw this rejection.

(4) The Examiner states that use of the phrase “harvestable parts” in claim 35 implies that some parts are not “harvestable.” Applicant have amended claim 35 to refer to a “leaf, stem, fruit, seed, or root” of a plant instead of “harvestable parts.” Thus, applicants have obviated the rejection.

(5) The Examiner states that claim 53(c) is unclear. Applicants have cancelled former claim 53, thereby obviating this rejection.

(6) The Examiner states that the phrase “the nucleic acid comprising” ... “the nucleic acid” in claim 71 is confusing. Applicants have cancelled claim 71, thereby obviating this rejection.

#### The Rejections Under 35 U.S.C. § 112, Written Description

The Examiner has rejected claims 29-35, 37, 48, 53-61, 64-69 and 71 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner has stated that the claims are drawn to “sequences that are at least 60% identical to SEQ ID NO: 1 that encodes a protein at least 60% identical to SEQ ID NO: 2 or to conservative variants thereof that have RdRP activity.” The Examiner contends, however, that the specification does not disclose what structural features would be conserved in the claimed sequences that would result in the claimed enzyme activity. The Examiner states that applicants are claiming a genus of sequences, yet there is no description of the structural features that define the genus. The Examiner cites *University of California v. Eli Lilly and Co.*, 43 USPQ 2d 1398 (Fed. Cir. 1997) (“Lilly”) for the proposition that the written description of an invention requires a precise structural and functional definition sufficient to distinguish it from other materials. Applicant traverses in view of the amendments to the claims, considered together with the following remarks.

Applicants have amended claims 29 and 31 to recite nucleic acid sequences that are at least 80% identical to SEQ ID NO: 1 or that encode a protein at least 80%

identical to SEQ ID NO: 2, and will address their response to the claims as amended. Contrary to the Examiner's assertion, the specification demonstrates that applicants had possession of the claimed invention. Further, the specification adequately describes the claimed transgenic plant cells and transgenic plants comprising the nucleic acid molecule of the invention. Specifically, applicants have demonstrated that they had possession of a number of nucleic acid molecules encoding an RdRP by Southern blot analysis of genomic DNA of potato, tobacco and two different varieties of tomato. See Example 5, page 41 of the specification and Fig. 2. The Southern blot reveals that the RdRP gene is present in each of the four genomes, providing evidence that the inventors had possession of a nucleic acid molecule encoding RdRP in various plant species. See Example 5, page 41 of the specification.

Applicants provide herewith a Declaration under 37 C.F.R. § 1.132 by Michael Wassenegger ("the Wassenegger declaration"), which states that the tobacco RdRP nucleotide sequence is 89.9 % identical to the coding region of the tomato RdRP nucleotide sequence exemplified in the instant application (SEQ ID NO: 1) and the tobacco RdRP amino acid sequence is 85.8 % identical to the coding region of the tomato RdRP nucleotide sequence exemplified in the instant application (SEQ ID NO: 2). See ¶6 of the Wassenegger Declaration. Thus, the Southern blot analysis showing that applicants had possession of a nucleic acid molecule encoding a tobacco RdRP combined with Wassenegger's declaration disclosing the sequence similarity of this molecule to that of SEQ ID NOS: 1 and 2 demonstrate that applicants had possession of the claimed genus at the time the invention was made.

In addition, the Examiner's reliance on Lilly is misplaced. Unlike Lilly, the nucleic acid molecules recited in the instant claims are structurally and functionally defined. The nucleic acid molecules are described structurally because they have a defined sequence identity to a nucleic acid molecule having the nucleotide sequence of SEQ ID NO: 1 or encoding the amino acid sequence of SEQ ID NO: 2. The nucleic acid molecules of the invention are described functionally as having RdRP activity or wherein the presence, transcription and/or expression of the nucleic acid molecule leads to a reduction of RdRP polypeptide synthesis. Thus, the specification describes the nucleic acid molecules recited in the claims by their physical properties. Further, Dr. Michael Wassenegger, who is an expert in the field (see, e.g., ¶1 of the Wassenegger Declaration) states that the written description in the specification sufficiently conveys the structural and physical features of the claimed transgenic plant cells and plants comprising nucleic acid molecules that have at least 80% sequence identity to SEQ ID NO: 1 or that encode a protein at least 80% identical to SEQ ID NO: 2 that result in the claimed RdRP activity. See ¶6 of the Wassenegger Declaration. Thus, the specification reasonably conveys to one of ordinary skill in the art that the inventor was in possession of the claimed genus at the time the application was filed.

#### The Rejection Under 35 U.S.C. § 112, Enablement

The Examiner has rejected claims 29-35, 37, 48, 53-61, 64-69 and 71 under 35 U.S.C. § 112, first paragraph. The Examiner contends that the specification, while being enabling for claims directed to a nucleic acid of SEQ ID NO: 1, or a nucleic acid encoding SEQ ID NO: 2, does not reasonably provide enablement for any sequences that are at least 60% identical to SEQ ID NO: 1, that encodes a protein at least 60% identical to SEQ ID



NO: 2 or to conservative variants thereof that have RdRP enzymatic activity. The Examiner contends that sequence homology is not sufficient to predict function of encoded sequences and refers to Doerks et al., TIG 14: 248-250 (1998) (hereafter, "Doerks"), Smith et al., Nature Biotechnology 15:1222-1223 (1997) (hereafter, "Smith"), Brenner, TIG 15:132-133 (1999) (hereafter, "Brenner") and Bork et al., TIG 12:425-427 (1996) (hereafter, "Bork") for support for this proposition.

The Examiner also asserts that the specification does not reasonably provide enablement for SEQ ID NO: 1 or a nucleic acid molecule encoding SEQ ID NO: 2 wherein the nucleic acid causes a reduction in synthesis of an RdRP. The Examiner states that applicants does not teach a reduction in synthesis of an RdRP in a plant cell. The Examiner contends that Ahlquist, Science 296:1270-1273 (2002) (hereafter, "Ahlquist") teaches that mechanisms for RdRP synthesis, regulation and degradation are not clear, and that Schiebel et al., Plant Cell 10:2087-2101(1998) (hereafter, "Schiebel") teaches that the biological functions of cellular RdRPs are not known. Applicants traverse in view of the amendments to the claims, considered together with the following remarks.

First, the Wassenegger Declaration demonstrates that a nucleic acid molecule exhibiting a sequence identity of approximately 80% or more to the nucleic acid molecules of this invention encodes a polypeptide with RdRP activity. The Wassenegger Declaration demonstrates that RdRP nucleic acid sequences from *Nicotiana tabacum* and *Arabidopsis thaliana* have been isolated, which have sequence identities of 89.9% and 63.2%, respectively, to the coding region of the tomato (SEQ ID NO: 1). See Exhibits 2-5 and ¶7 of the Wassenegger Declaration. The Wassenegger Declaration also shows that amino acid

sequences encoding RdRP from *Nicotiana tabacum* and *Arabidopsis thaliana* have sequence identities of 85.8% and 61.9%, respectively, to that of the tomato (SEQ ID NO: 2). *Id.* Further, Wassenegger notes that Xie et al. (PNAS, 99:6516-6521, 2001; hereafter "Xie") has demonstrated that the nucleic acid molecule encoding the *N. tabacum* RdRP (NtRdRP) has RdRP activity. See, e.g., pages 6517-6519 of Xie. Thus, given the teachings in the specification as filed, one skilled in the art could make and use nucleic acid molecules that exhibit a sequence identity of at least 80% to SEQ ID NO: 1 or that encode a protein that is at least 80% identical to SEQ ID NO: 2 without undue experimentation.

Second, the Examiner's reliance on Doerks, Smith, Brenner and Bork is misplaced because all of them are concerned with the use of automated assignment of function to genomic sequences. This problem is not relevant to applicants' invention. For example, Doerks is concerned with how the use of automatic software robots to assign function to genome sequences can lead to errors in the assigned function. See, e.g., page 248, left column of Doerks. Similarly, Smith is concerned with using sequence similarity methods "when applied in an automated manner to large data sets with minimum review" (See Smith, page 1222, left column). Both Brenner and Bork are also only pertinent to automated function analysis. Further, both Doerks and Smith indicate that sequence similarity do provide functional information if used with either researcher input or more sophisticated methods. For example, Doerks indicates that functional annotation was provided for more than 700 of about 1300 proteins based upon sequence similarities (see page 250, left column of Doerks), while Smith states that using sequence similarity methods are "a generalization of *successful* approaches used by many researchers to assign probable functions to new sequences when previously studied and recognized homologs exist." (see

Smith, page 1222, left column) emphasis added. Thus, none of Doerks, Smith, Brenner and Bork is relevant for the applicants' claimed invention.

Third, contrary to the Examiner's assertion, the specification also discloses how one of ordinary skill in the art can determine, using only routine experimentation, whether a protein encoded by a nucleic acid molecule of the invention has RdRP activity. See page 31, line 19-31 of the specification. The specification also discloses that expression of a nucleic acid molecule of the invention in a plant cell would reduce the synthesis of a polypeptide having RdRP activity due to an antisense or co-suppression effect. See page 22, lines 6-12 of the specification. Specifically, the specification teaches how to make transgenic plant cells and plants, such that one of ordinary skill in the art could make the claimed plant cells and plants without undue experimentation. See, e.g., page 23, line 27 to page 25, line 13 of the specification. Further, the specification also discloses how one of ordinary skill in the art can determine, using only routine experimentation, whether a protein encoded by a nucleic acid molecule of the invention has RdRP activity. See page 31, line 19-31 of the specification. Therefore, the specification enables the claimed transgenic plant cells.

In addition, the Wassenegger Declaration demonstrates that one skilled in the art, following the teachings of the specification, could identify nucleic acid molecules encoding RdRP following the teachings of the specification (see ¶8 of Wassenegger Declaration). The Wassenegger Declaration also shows that one skilled in the art could make and use transgenic plants and plant cells containing the nucleic acid molecules of the invention, including those in which the integrated constructs would reduce RdRP activity in

the cell. See ¶¶9-13 of Wassenegger Declaration. Specifically, Xie has demonstrated that expression of a homologous RdRP nucleic acid molecule in an antisense orientation reduces RdRP activity using methods that are taught by the specification. See ¶¶10-11 of Wassenegger Declaration. Further, the Wassenegger Declaration describes experiments demonstrating the production of transgenic tobacco plants with an integrated heterologous nucleic acid molecules encoding RdRP in antisense orientation that show reduced RdRP activity. See ¶12 of Wassenegger Declaration. In addition, as Dr. Wassenegger states, it was well known at the time the invention was made that co-suppression could be used to reduce the expression of a gene in a plant. It is noted that an absence of a working example “should never be the sole reason for rejecting the claimed invention on the grounds of lack of enablement.” See, MPEP 2164.02. Thus, given the teaching of the specification, one of ordinary skill in the art could produce a transgenic plant comprising an antisense RdRP or an RdRP that has been co-suppressed and that displays reduced RdRP activity.

Finally, Ahlquist and Schiebel are irrelevant to whether the claimed invention is enabled. Ahlquist clearly states that cellular RdRPs are involved in copying messenger RNA templates and in the intercellular spread of amplified sequences (see abstract, page 1270 of Ahlquist). Ahlquist also states that cellular RdRPs function in, *inter alia*, RNA silencing and plant antiviral activity, even though the exact mechanism of RdRP action in RNA silencing is unclear (see pages 1272-73 of Ahlquist). Similarly, Schiebel demonstrates that a nucleic acid molecule encoding RdRP has RNA-directed RNA polymerase activity and shows that RdRP mRNA is increased upon virus infection (see abstract, page 2087 of Schiebel). There is no requirement that the exact mechanism of action be known in order to make and/or use an invention. See, e.g., *In re Cortright* 49

USPQ2d 1464, 1469 (holding that it is not a requirement of patentability that an inventor knows how or why an invention works). In this case, applicants have taught in the specification that RdRP may be reduced in a transgenic plant or plant cell by, e.g., antisense or co-suppression methods, and they and others have subsequently made such transgenic plants.

#### The Rejections Under 35 U.S.C. § 102

The Examiner has rejected claims 29-35, 37, 53-61 and 64-69 rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Fischhoff et al., United States Patent 5,495,071, issued February 27, 1996 (hereafter "Fischhoff"). The Examiner states that the above claims are drawn to nucleic acids encoding polypeptides having RdRP activity, related nucleic acids and parts thereof, transgenic plant cells, transgenic plants, and propagation material. The Examiner states that the Office interprets "a part" of a DNA sequence to be a single base. The Examiner contends that Fischhoff teaches a tomato plant transgenic for a *Bacillus thuringiensis* toxin protein gene and that the tomato plant inherently has a tomato RdRP coding sequence. The Examiner states that since the tomato plant taught by Fischhoff is transgenic for a heterologous gene, a single base of Fischhoff anticipates the claimed invention. Applicants traverse in light of the amended claims.

Applicants have amended claims 29 and 31 to recite that the nucleic acid integrated in to the genome of the transgenic plant cell is a "foreign" nucleic acid. The disclosure of the application states that

"[b]y foreign it is meant that the nucleic acid molecule is either heterologous with respect to the host cell which means that said nucleic acid

molecule is derived from a cell or organism with a different genomic background, or that is homologous with respect to the host cell but located in a different genomic environment than the naturally occurring counterpart of said nucleic acid molecule. This means that, if the nucleic acid molecule is homologous with respect to the host cell, it is not located in its natural location in the genome of said host cell.

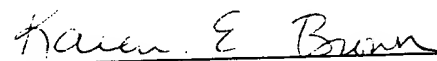
See specification at page 10, lines 19-26. Fischhoff does not teach or suggest a transgenic plant comprising a foreign nucleic acid molecule of the invention. Thus, applicants have obviated the rejection.

The Examiner states that claim 71 is rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Poovaiah, et al., United States Patent 5,498,533, issued March 12, 1996 (hereafter "Poovaiah"). The Examiner contends that Poovaiah teaches a plant transgenic for a DNA sequence (Poovaiah's SEQ ID NO: 1) which has 29 contiguous nucleotides identical to SEQ ID NO: 1 of the claimed invention. As discussed above, applicants have cancelled claim 71, rendering this objection moot.

Conclusion

In view of the foregoing amendments and remarks, applicant requests that the Examiner withdraw the claim rejections and allow all claims of this application. If the Examiner believes that an interview would facilitate the resolution of any outstanding issues, he is kindly requested to contact the undersigned.

Respectfully submitted,



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IN THE CLAIMS

✓ Please cancel claims 40-41, 53-63 and 71.

✓ Please amend claims 29-32, 35 and 37 as follows:

AMENDED

per

29. (Twice Amended) An isolated transgenic plant cell comprising a foreign nucleic acid molecule stably integrated into the genome, wherein the nucleic acid molecule is a nucleic acid molecule encoding a polypeptide having the enzymatic activity of an RNA-directed RNA polymerase (RdRP) or encoding an enzymatically active fragment thereof, selected from the group consisting of:

- (1) a nucleic acid molecule coding for a polypeptide comprising the amino acid sequence of SEQ ID NO: 2;
- (2) a nucleic acid molecule comprising the coding region of the nucleotide sequence of SEQ ID NO: 1;
- (3) a nucleic acid molecule that specifically hybridizes to a complementary strand of the nucleic acid molecule as defined in (1) or (2) in 0.25 M NaHPO<sub>4</sub> pH 7.2; 0.25 M NaCl, 7% SDS, 1 mM EDTA and 5-20% (w/v) polyethylene glycol ( $M_r$  6-7.5x10<sup>3</sup>) at 42° C for 4-24 hours; and
- (4) a nucleic acid molecule that has a sequence identity of at least 80% to the nucleic acid molecule of (1) or (2);

wherein said nucleic acid molecule is linked to regulatory elements allowing transcription, expression, or transcription and expression of said nucleic acid molecule in plant cells.



AMENDED

per E

30. (Twice Amended) A transgenic plant comprising the plant cell of any one of claims 29 or 64-70.

AMENDED

per E

31. (Twice Amended) An isolated transgenic plant cell which contains stably integrated into the genome a foreign nucleic acid molecule selected from the group consisting of:

- (1) a nucleic acid molecule coding for a polypeptide comprising the amino acid sequence of SEQ ID NO: 2;
- (2) a nucleic acid molecule comprising the coding region of the nucleotide sequence of SEQ ID NO: 1;
- (3) a nucleic acid molecule that specifically hybridizes to a complementary strand of the nucleic acid molecule as defined in (1) or (2) in 0.25 M NaHPO<sub>4</sub> pH 7.2; 0.25 M NaCl, 7% SDS, 1 mM EDTA and 5-20% (w/v) polyethylene glycol ( $M_r$  6-7.5x10<sup>3</sup>) at 42° C for 4-24 hours; and
- (4) a nucleic acid molecule that has a sequence identity of at least 80% to the nucleic acid molecule of (1) or (2);

wherein said nucleic acid molecule is linked to regulatory elements allowing transcription, expression, or transcription and expression of said nucleic acid molecule in plant cells; and

wherein the presence, transcription, expression, or transcription and expression of the nucleic acid molecule leads to reduction of the synthesis of a polypeptide having RNA-directed RNA polymerase (RdRP) activity in the cell.

AMENDED

per E

32. (Amended) The transgenic plant cell of claim 31, wherein the reduction is achieved by an antisense or co-suppression effect.

AMENDED

per E

35. (Twice Amended) A leaf, stem, fruit, seed, or root of a plant, wherein said leaf, stem, fruit, seed, or root comprises the plant cell according to any one of claims 29, 31 or 32.

AMENDED

per E

37. (Twice Amended) Propagation material of a plant, wherein said propagation material comprises the plant cell according to any one of claims 29, 31 or 32.

✓ Please add claims 72-74:

ADDED

per E

72. (Added) An isolated transgenic plant cell comprising a foreign nucleic acid molecule stably integrated into the genome, wherein the nucleic acid molecule is a nucleic acid molecule coding for an RNA molecule that is capable of serving as a template for RNA-directed RNA synthesis, wherein said template nucleic acid molecule is linked to regulatory elements allowing transcription of said template nucleic acid molecule in plant cells.

ADDED

per E

73. (Added) The isolated transgenic plant cell according to claim 31, wherein said foreign nucleic acid molecule has a sequence identity of at least 90% to (1) a nucleic acid molecule coding for a polypeptide comprising the amino acid sequence of SEQ ID NO: 2; or (2) a nucleic acid molecule comprising the coding region of the nucleotide sequence of SEQ ID NO: 1.

ADDED

per E

74. (Added) The isolated transgenic plant cell according to claim 73, wherein said foreign nucleic acid molecule is (1) a nucleic acid molecule coding for a

## APPENDIX OF AMENDMENTS

29. (Twice Amended) An isolated transgenic plant cell comprising a foreign nucleic acid molecule stably integrated into the genome, wherein the nucleic acid molecule is[: (a) ] a nucleic acid molecule encoding a polypeptide having the enzymatic activity of an RNA-directed RNA polymerase (RdRP) or encoding an enzymatically active fragment thereof, selected from the group consisting of:

(1) a nucleic acid molecule coding for a polypeptide comprising the amino acid sequence of SEQ ID NO: 2;

(2) a nucleic acid molecule comprising the coding region of the nucleotide sequence of SEQ ID NO: 1;

(3) a nucleic acid molecule that specifically hybridizes to a complementary strand of the nucleic acid molecule as defined in (1) or (2) in 0.25 M NaHPO<sub>4</sub> pH 7.2; 0.25 M NaCl, 7% SDS, 1 mM EDTA and 5-20% (w/v) polyethylene glycol (M<sub>r</sub> 6-7.5x10<sup>3</sup>) at 42° C for 4-24 hours; and

(4) a nucleic acid molecule that has a sequence identity of at least [60%] 80% to the nucleic acid molecule of (1) or (2); [and

(5) a nucleic acid molecule, the nucleotide sequence of which is degenerate as a result of the genetic code to a nucleotide sequence of the nucleic acid molecule as defined in (3) or (4);]

wherein said nucleic acid molecule is linked to regulatory elements allowing transcription, [and/or] expression or transcription and expression of said nucleic acid molecule in plant cells; [; and/or

(b) a template nucleic acid molecule coding for an RNA molecule that is capable of serving as a template for RNA-directed RNA synthesis, wherein said nucleic acid molecule is linked to regulatory elements allowing transcription of said nucleic acid molecule in plant cells.]

30. (Twice Amended) A transgenic plant comprising the plant cell of any one of claims 29 or [65-71] 64-70.

31. (Twice Amended) An isolated transgenic plant cell which contains stably integrated into the genome a foreign nucleic acid molecule selected from the group consisting of:

- (1) a nucleic acid molecule coding for a polypeptide comprising the amino acid sequence of SEQ ID NO: 2;
- (2) a nucleic acid molecule comprising the coding region of the nucleotide sequence of SEQ ID NO: 1;
- (3) a nucleic acid molecule that specifically hybridizes to a complementary strand of the nucleic acid molecule as defined in (1) or (2) in 0.25 M NaHPO<sub>4</sub> pH 7.2; 0.25 M NaCl, 7% SDS, 1 mM EDTA and 5-20% (w/v) polyethylene glycol (M<sub>r</sub> 6-7.5x10<sup>3</sup>) at 42° C for 4-24 hours; and
- (4) a nucleic acid molecule that has a sequence identity of at least [60%] 80% to the nucleic acid molecule of (1) or (2); [and
- (5) a nucleic acid molecule, the nucleotide sequence of which is

degenerate as a result of the genetic code to a nucleotide sequence of the nucleic acid molecule as defined in (3) or (4); and

(6) a nucleic acid molecule comprising at least 15 contiguous nucleotides of any of (1) - (5) or a complementary strand thereof;]

wherein said nucleic acid molecule is linked to regulatory elements allowing transcription, [and/or] expression, or transcription and expression of said nucleic acid molecule in plant cells; and

wherein the presence, transcription, [and/or] expression, or transcription and expression of the nucleic acid molecule leads to reduction of the synthesis of a polypeptide having RNA-directed RNA polymerase (RdRP) activity in the cell.

32. (Amended) The transgenic plant cell of claim 31, wherein the reduction is achieved by an antisense [, ribozyme and/or] or co-suppression effect.

35. (Twice Amended) [Harvestable parts] A leaf, stem, fruit, seed, or root of a plant, wherein said leaf, stem, fruit, seed, or root [comprising] comprises the plant cell according to any one of claims 29, 31 or 32.

37. (Twice Amended) Propagation material of a plant, wherein said propagation material [comprising] comprises the plant cell according to any one of claims 29, 31 or 32.